

**UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY
CAMDEN VICINAGE**

**IN RE: VALSARTAN, LOSARTAN,
AND IRBESARTAN PRODUCTS
LIABILITY LITIGATION**

This Document Relates to All Actions

MDL No. 2875

Honorable Robert B. Kugler,
District Court Judge

**BRIEF IN SUPPORT OF DEFENDANTS' JOINT MOTION FOR
CLARIFICATION REGARDING *DAUBERT* HEARING ORDER 1**

INTRODUCTION

Defendants seek clarification with regard to the scope of testimony Drs. Lagana and Hecht are permitted to offer at trial regarding NDEA. Pursuant to *Daubert* Order 1, [Dkt. 1958](#), the Court granted Defendants' motions to preclude the testimony of Plaintiffs' experts Dipak Panigrahy and Mahyar Etminan concerning NDEA and causation of all cancers other than pancreatic. Further, the Court granted Defendants' Motion to Preclude Testimony of Plaintiffs' expert David Madigan concerning NDEA and all cancer causation. The Court denied Defendants' motions to preclude Plaintiffs' experts Stephen Lagana and Stephen Hecht, but its written Order did not address NDEA with respect to these experts.

As the Court is aware, Drs. Lagana and Hecht—unlike Drs. Panigrahy, Etminan, and Madigan—did not perform a cancer-by-cancer analysis regarding

NDEA. Instead, they primarily focused on NDMA studies and only offered opinions regarding nitrosamines and “cancer,” in general. Further, neither Dr. Lagana nor Dr. Hecht considered any relevant scientific evidence that is different than the literature considered by Drs. Panigrahy and Etminan such that it would justify permitting Drs. Lagana and Hecht to offer NDEA opinions broader than Plaintiffs’ other experts.

It follows that the reason the Court did not expressly limit the opinions of Drs. Lagana or Hecht concerning NDEA to a specific cancer or set of cancers was because those experts do not even offer such opinions, nor do they cite to scientific evidence that would support such testimony. Nevertheless, to avoid any ambiguity as to the permissible scope of Plaintiffs’ general causation expert opinions, Defendants respectfully ask the Court to clarify that Drs. Lagana and Hecht are *not* permitted to offer testimony at trial linking NDEA to *any* specific cancers because this is beyond the scope of their reports and the evidence they reply upon.

DISCUSSION

A. Drs. Lagana and Hecht focused on NDMA and did not offer opinions regarding NDEA and specific cancer types.

Plaintiffs initially identified 13 categories of cancer at issue in this litigation. [Dkt. 706](#). Their general-causation experts, however, support, at most, ten cancer categories. *See, e.g.*, Panigrahy Rep. at 96-147; Etminan Rep. at 16-24; Madigan Rep. at 9. Although each of Plaintiffs’ experts performed a literature review to

formulate their opinions, the breadth and scope of their reports vary dramatically. On one end of the spectrum, Dr. Panigrahy purported to have reviewed all relevant literature—including animal studies, dietary studies, cohort studies, epidemiological studies, and *in vitro*/mechanistic studies—to offer opinions regarding the potential association between NDMA, NDEA, and specific categories of cancer. Along the same lines, Dr. Etminan described his methodology as “a systematic search of the scientific evidence” to determine whether nitrosamine impurities in valsartan “increase the risk of different types of cancer.” Etminan Rep. at 3. In contrast, Drs. Lagana and Hecht attempted to establish a more generalized association between NDMA and “cancer,” which they suggest would also apply to NDEA. Finally, Dr. Madigan did not opine on causation at all, but performed a statistical analysis in support of Dr. Etminan’s literature review.

These distinctions necessarily informed the Court’s rulings set forth in *Daubert* Order 1. Indeed, unlike Drs. Panigrahy and Etminan, Drs. Lagana and Hecht did not focus on NDEA nor did they offer opinions regarding an association between NDEA and specific cancer types. Dr. Lagana acknowledged that his “discussion of the contaminated valsartan is focused primarily on NDMA studies,” though he suggested that “the discussion applies to NDEA as well.” Lagana Rep. at 1. Thus, Dr. Lagana departed from Drs. Panigrahy and Etminan insofar as he did not attempt to perform any independent assessment of NDEA as a distinct chemical

compound. In rendering this opinion, Dr. Lagana “discussed the mechanism by which NDMA causes cancer . . . summarized compelling evidence for relatively small amounts of NDMA (dietary ingestion) causing cancer in human adults,” assessed certain documents and testimony from the Defendants, and provided an overview of the animal studies. Lagana Rep. at 29-32. He did not, however, conduct a particularized assessment of the organs that might be susceptible to developing cancer due to NDEA (or even NDMA) exposure, nor did he analyze each of the cancer types alleged by Plaintiffs to be at issue.

Similarly, Dr. Hecht’s analysis also was focused on the broader concepts of “cancer” causation. He concluded that the presence of nitrosamine impurities in affected valsartan “caused an unreasonably dangerous and unacceptable risk of causing or substantially contributing to the causation of cancer for those ingesting the valsartan.” Hecht Rep. at 27. While Dr. Hecht noted that “a range of cancers have been associated with intake of NDMA (and NDEA by extension),” he did not attempt to perform an assessment of specific cancers related to either NDMA or NDEA. Hecht Rep. at 27. Thus, like Dr. Lagana, Dr. Hecht did little in the way of an independent NDEA analysis in reaching his opinions, and he did not offer the opinion that NDEA causes any particular category of cancer in humans.¹

¹ Dr. Hecht’s report also contains several liability opinions, which the parties agree are not presently at issue.

In contrast to the high-level approach adopted by Drs. Lagana and Hecht, Drs. Panigrahy and Etminan conducted an examination of the literature for an association between NDMA *and* NDEA as related to specific cancers. Dr. Panigrahy's cancer-by-cancer analysis with regard to NDMA spanned over 50 pages of his report. Panigrahy Rep. 96-148. Dr. Panigrahy also conducted a cancer-by-cancer assessment of NDEA, though it was much more limited and supported primarily by animal data as opposed to human epidemiological evidence. Panigrahy Rep at 182-194. Finally—unlike Plaintiffs' other experts—Dr. Panigrahy at least attempted to justify his assertion that one can extrapolate the results of an NDMA study and apply it to NDEA. Panigrahy Rep. at 177-178. Even so, the Court precluded Dr. Panigrahy from testifying about an association between NDEA and all cancers other than pancreatic. *Daubert* Order 1, [Dkt. 1958](#), at 2.

Dr. Etminan is situated similarly. He devoted the majority of his report to a review of the epidemiological data from occupational and dietary studies that he believes supports causation of cancers in specific organs due to NDMA and NDEA exposure. Etminan Rep. at 13-24. As the Court determined, Dr. Etminan conducted “a thorough review” of the available literature. Day 1 Hrg. Tr. at 156. Dr. Madigan then attempted to lend further support to Dr. Etminan's effort by calculating lifetime cumulative exposures to NDMA and NDEA in the key studies relied upon by Dr. Etminan. Despite this, Dr. Etminan is limited to testifying about an association

between NDEA and pancreatic cancer, and Dr. Madigan is precluded from offering any NDEA-related opinions whatsoever. *Daubert* Order 1, [Dkt. 1958](#), at 2.

Plaintiffs' general causation experts undertook different assignments given their varied backgrounds and experience. These differences define the scope of their opinions and necessarily constrain the testimony that they are permitted to offer to a jury. Accordingly, it would be inconsistent with the Court's ruling if, based on their more limited analyses Drs. Lagana and Hecht were permitted to offer opinions at trial regarding NDEA and specific cancer types when (i) they never offered those opinions in the first place, and (ii) Drs. Panigrahy, Etminan, and Madigan—who did purport to perform the requisite analysis—will not be permitted to do so.

While this may be self-evident based on the Court's statements on the record and in *Daubert* Order 1, in an effort to avoid any ambiguity concerning the permissible scope of Drs. Lagana and Hecht's expert opinions, Defendants seek confirmation that they will not be permitted to testify that NDEA can cause any of the 13 types of cancer disclosed by Plaintiffs.

B. Drs. Lagana and Hecht did not rely on any new or different scientific evidence as Plaintiffs' other experts regarding the alleged association between NDEA and cancer.

Plaintiffs' general causation experts all employed a similar methodology in forming their opinions. They conducted a literature review and then assessed the weight of the evidence. Day 1 Hrg. Tr. at 154 (stating, "[t]he methodology [Dr.

Hecht] uses is the same as everyone else, he examines all the studies that are available, he explains why he thought some were not terribly helpful or relevant and why some were”).

As a byproduct of this homogenous approach, each of Plaintiffs’ experts borrowed from the same common body of literature to support their conclusions. With regard to NDEA, however, the evidence was sparse. This Court recognized as much in precluding Plaintiffs’ experts from opining on an association between NDEA and cancer, beyond pancreatic cancer. Specifically, Dr. Etminan cites only to the Zheng paper in support of a causal association between NDEA and cancer. As a result, the Court held that “[Dr. Etminan] can express an opinion as to the association between NDEA and pancreatic cancer because that’s the only data apparently that’s available[.]” Day 1 Hrg. Tr. at 152-53. Likewise, Dr. Panigrahy—whose citation list numbered almost 600—similarly relied only on Zheng to establish an association between NDEA and a single cancer. As a result, the Court limited Dr. Panigrahy’s testimony concerning NDEA as well: “As to the opinions of Dipak Panigrahy, M.D., which concern NDMA and all cancers as well as NDEA and pancreatic cancer, Defendant’s Motion to Preclude is DENIED; as to the opinions of [Dr. Panigrahy] which concern NDEA and all other cancers, Defendant’s Motion to Preclude is GRANTED.” *Daubert* Order 1, [Dkt. 1958](#), at 2.

Neither Dr. Lagana nor Dr. Hecht break any new ground concerning NDEA and cancer causation that would merit a different result or otherwise permit them to offer opinions the Court has already excluded. Apart from his citation to the Zheng study, Dr. Lagana identifies no meaningful evidence that would support an association between NDEA and any of the cancers Plaintiffs have alleged to be at issue. Indeed, Dr. Lagana cites only two papers—Thresher and Choi—that are not also referenced by Drs. Panigrahy and/or Etminan.² Neither paper supports an association between NDEA and cancer causation in specific organs. Further, when Dr. Lagana was asked at his deposition to identify any evidence of which he is aware to support causation of NDMA or NDEA with regard to specific cancers, he merely cited to the dietary and animal studies referenced in his report—all of which were also discussed by Dr. Panigrahy, Dr. Etminan, or both. Lagana Dep. at 376:2-377:3.

Similarly, Dr. Hecht cited only three sources concerning NDEA that were not also considered by either Dr. Panigrahy or Dr. Etminan. These are an American Chemical Society monograph circa 1984³ and the Hecht and Tricker papers.⁴ Again, none of these materials supports an association between NDEA at relevant levels

² Copies of the Thresher and Choi papers are contained within Appendix A to the Certification of Clem C. Trischler.

³ Preussmann, R., and Stewart, B.W. (1984) N-Nitroso Carcinogens, In Chemical Carcinogenesis, Second Edition, ACS Monograph 182 (Searle, C. E., Ed.), American Chemical Society, Washington, DC.

⁴ Copies of the Hecht and Tricker papers are contained within Appendix B to the Certification of Clem C. Trischler.

and any specific cancer. Moreover, Dr. Hecht's report does not cite to Zheng, the sole evidence identified by Drs. Panigrahy and Etminan to support a causal association between NDEA and one specific cancer in humans. Based on his deposition testimony, Dr. Hecht was either unaware of this study or did not find it persuasive:

Q: It's never been written anywhere in the scientific literature that dietary exposure to NDEA has caused cancer in humans, has it?

A. Now you're on NDEA?

Q. Yes.

A. Okay. I thought you were talking about NDMA. ***I do not believe that there is such a study, yes, where it says NDEA caused cancer in humans. I don't think there is such a study in the literature.***

* * *

Q: ***If we listed all 13 of the cancers that are at issue, are you aware of any peer-reviewed study that concluded that exogenous intake of NDEA was the cause of any of those cancers?***

A. ***No.***

Hecht Dep. at 246:23-247:1; 256:14-19 (emphasis supplied).

Considering the Court limited the scope of both Dr. Panigrahy's and Dr. Etminan's opinions regarding NDEA to pancreatic cancer based on a lack of available evidence, it would be inconsistent—in fact, anomalous—to permit Drs. Lagana and Hecht to testify as to a wider range of specific cancers when they didn't even purport to offer those opinions in the first instance and, moreover, they do not

cite to any new or different literature beyond what the Court has already found insufficient to connect NDEA to 12 of the 13 cancers listed in their disclosure.

CONCLUSION

In order to avoid any confusion or ambiguity, Defendants respectfully request that the Court clarify its ruling and expressly confirm that Drs. Hecht and Lagana are precluded from offering any opinions at trial regarding NDEA and specific cancers.

Dated: March 18, 2022

Respectfully Submitted:

By: /s/ Clem C. Trischler

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CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on March 18, 2022, I electronically filed the foregoing with the Clerk of the Court by using the CM/ECF system which will send a notice of electronic filing to all CM/ECF participants in this matter.

/s/ Clem C. Trischler

Clem C. Trischler